1970 ANNUAL REPORT

PHARMACEUTICAL MANUFACTURERS ASSOCIATION FOUNDATION, INC.

THE FIRST 5 YEARS—BUILDING FOR TOMORROW
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Mid-1966 serves well as a beginning point from which to review the record of the PMA Foundation's first five years. By then the Scientific Advisory Committee had been formed, guidelines governing the distribution of Foundation funds were well on the way to being developed by the Board of Directors, contributions had reached a level where funds could be committed for program support, and the flow of applications from the scientific community was beginning to be substantial.

These five years embrace a significant record, both in the quality and quantity of efforts supported with the slightly more than $2.8 million generously contributed. These funds have gone into a number of programs which fall within the Foundation's guidelines of: (a) support for fundamental research in toxicology, (b) support for research and personnel in the field of clinical pharmacology and drug evaluation.

At the end of 1970:
- 80 awards have been made under a program aimed at interesting medical students in clinical pharmacology as a career.
- 19 medical school faculty members have been awarded two years (some three years) of salary support under a program in clinical pharmacology.
- 10 fellowship awards have been made under a unique program aimed at promoting a whole new interdisciplinary approach to drug research by combining the skills and techniques of the fields of pharmacology and morphology.
- 23 research grants have been awarded in a variety of areas within the guidelines.
- 20 workshops and conferences have been supported which range in subject matter from the basic principles of drug metabolism to the principles of drug evaluation in man.
- Three publications have been supported: in drug metabolism, in recruitment to careers in pharmacology, and in the preparation of a textbook dealing with the principles of pharmacology for the nonprofessional.

What of the accomplishments? The medical student program of traineeships in clinical pharmacology has proven to be highly successful. The hoped-for result from this program is that students will retain an interest in clinical pharmacology and choose the field as a career. Information on 45 of the 56 students who had received awards prior to the 1970 awards show that 30 students have continued their interests in the field following the conclusion of the Foundation award. Some have now gone on to programs in this specialty at the National Institutes of Health or are in medical residency programs, focusing on the clinical pharmacology needs of that particular field. Others still in medical school continue to extend the research begun during the Foundation award. These early successes reinforce the belief of the Board of Directors that this program meets a real need.
Since the first faculty development awards in clinical pharmacology in 1967, 19 faculty members have received support under this program, with six of these awards to begin in 1971. A most important measure of success is whether these scientists have remained in the field of clinical pharmacology. Eleven of the first thirteen awardees are still engaged in it full-time, with four in the field today only because of the Foundation award. The likelihood is quite strong that these eleven will continue their careers actively engaged in clinical pharmacology concerns.

A unique fellowship program in pharmacology-morphology shows promise of firmly establishing this new interdisciplinary dimension to pharmacologic research. Like the faculty awards program, it must have the benefit of a longer-range perspective for a full evaluation. However, on the basis of the first three years of the program, the Foundation indeed looks to an ever-growing demand for these awards and a progressively increasing awareness by the scientific community of the program's importance. Of the ten fellowships awarded, five were made in 1970. An important event flowing from one of the fellowships was that one university instituted a program to provide the opportunity for other scientists interested in this interdisciplinary field to follow their inclinations.

Some important and interesting research efforts have been supported. Support has gone to ongoing efforts at critical times when programs were in danger of having to be terminated for lack of continuing funds. Other grants have enabled established investigators to extend their interests into fields of concern to the Foundation. Still others have been starter grants which have resulted in ongoing research programs. A precise measure of the Foundation's role is more difficult to construct in its research program than in its educational programs. Each research grant, in its own way, represents an opportunity to add to the growing and basic body of knowledge of the science of therapeutics.

Five years is a fairly substantial span of time. Measurable results of achievements during this time have been noted. These early results demonstrate that the Foundation has firmly established itself as an organization committed to the support of innovative programs.

Five years is also a short period of time. To fully measure the impact of programs supported by the Foundation, a longer time period is necessary. What happens to these early successes over a longer period will be vitally important to the Foundation in the years ahead. It is on the strengths of the Foundation's early efforts that the programs for tomorrow will be built.

With large foundations and federal sources providing substantial support in biomedical research, the Foundation has deftly identified important areas into which it directs funds. It is confident the future holds an extension of its early progress. Implicit in this belief is that the Foundation will continue to merit the confidence of its many financial supporters, that the excellent advice provided in the past by the advisory committee will continue, and that the various members of the scientific community will continue to submit many well-conceived applications for support.
Since its formation, approximately $3,000,000 has been authorized by the PMA Foundation for a variety of workshops, conferences, research projects and educational programs. The Foundation truly represents the national concern of its supporters in promoting the science of therapeutics. This section describes highlights of the various activities supported during the year.

**Workshops and Conferences**

Workshops and conferences are important educational devices. Since support for the first workshop in drug metabolism was authorized by the Foundation in late 1965, a number of pertinent meetings have continued to receive support.

**Adverse Reactions.** An International Conference on Adverse Reactions Reporting Systems was held October 22-23, 1970, at the United States Department of Commerce in Washington, D.C. The conference was under the chairmanship of John A. Oates, M.D., Professor of Medicine and Pharmacology, Vanderbilt University, School of Medicine. The PMA Foundation provided partial support for the meeting through an enabling grant of $6,000 to the Drug Research Board, National Academy of Science-National Research Council. Other sponsors were the National Academy of Sciences-National Research Council, the Food and Drug Administration, the National Cancer Institute, the National Institute of Child Health and Human Development, National Institute of General Medical Sciences, NIH, and the Registry of Tissue Reactions to Drugs.

The purpose of the conference was to examine the methods of gathering and evaluating data on adverse reactions to drugs. With the aid of speakers from the United States and other countries with well-developed reporting systems, the conference reviewed the main elements of useful adverse reaction reporting structures. The meeting was open to all.

**Clinical Pharmacology.** A Second Workshop on the Principles of Drug Evaluation in Man was held June 15-19, 1970 at the University of Kansas Medical Center in Kansas City, Kansas. The workshop director was Daniel L. Azarnoff, M.D., Professor of Medicine and Pharmacology, University of Kansas.

Sponsors for the meeting were the Drug Research Board, National Academy of Sciences-National Research Council, the PMA Foundation, The National Institute of General Medical Services, NIH, and the University of Kansas Medical Center. The enabling grant of $21,000 was made by the PMA Foundation.

A Conference on Clinical Pharmacology, held in Washington on December 3-4, 1970, was co-sponsored by the PMA Foundation. No funds were requested from the Foundation for this meeting. The purpose of this conference was to bring together knowledgeable scientists from the pharmaceutical industry, government and schools of medicine to assess the current status and project the future needs in clinical pharmacology. In addition to the Foundation, the following were the sponsors: The Drug Research Board, National Academy of Sciences-National
Participants in a laboratory session held at the training program for pharmacology doctorate candidates at the College of Physicians and Surgeons, Columbia University in July, 1970.

Research Council, the American Society for Clinical Pharmacology and Therapeutics; the American Society for Pharmacology and Experimental Therapeutics; the Food and Drug Administration, the National Institute of General Medical Sciences, and the Veterans Administration. The Chairman was Leon L. Goldberg, Ph.D., M.D., Professor of Pharmacology and Internal Medicine, Emory University School of Medicine. The meeting was open to all who wished to attend.

An award of $176,880 was made to support a four-year effort by the American Society of Pharmacology and Experimental Therapeutics directed at advanced pharmacology students. The funds support four to six week courses for Ph.D. candidates at selected universities where highly specialized studies are offered. Through this award, training in pharmacology for these selected doctorate candidates is enhanced in departments which are very capable in certain subject areas. Up to 50 doctoral candidates can be accommodated each year. The American Foundation for Pharmaceutical Education also has provided financial support for this activity.

The first host was the University of Minnesota, Department of Pharmacology, and the director was Gilbert J. Mannering, Ph.D., Professor of Pharmacology. This session was held in 1969 for four weeks and dealt with drug metabolism and biochemical pharmacology.

The second location was the College of Physicians and Surgeons, Columbia University, New York City for four weeks beginning July 6, 1970. The director was Brian F. Hoffman, M.D., Chairman, Department of Pharmacology. The area of instruction was cardiovascular pharmacology.

The last two sessions currently funded, will be hosted in 1971 by the University of California, San Francisco, Department of Pharmacology; and in 1972 by Vanderbilt University, Department of Pharmacology. The courses will deal with neuropharmacology and psychopharmacology.

Mutagenicity. A Conference on Evaluating Mutagenicity of Drugs and Other Chemical Agents was held November 4-6, 1970, at the Department of State, Washington, D.C. Drs. Paul Calabresi, Physician-in-Chief, Rogers Williams, General Hospital, and Alexander Hollaender, Biology Division, Oakridge National Laboratory, were co-chairmen. The PMA Foundation provided partial support with a grant of $5,000. Other co-sponsors of the conference were the Drug Research Board, the National Academy of Science-National Research Council, the Environmental Mutagen Society, the Food and Drug Administration, and the National Institute of General Medical Sciences.

The conference provided the opportunity to discuss the possible mutagenicity of drugs and other chemicals. With the considerable number of tests which have been developed to predict mutagenic effects, a problem exists at present to determine their validity and particularly to demonstrate if mutagenicity in vitro and in animals carries with it implications for mutagenicity in man. The meeting was open to all.
Pediatric Pharmacology. A grant of $1,000 was provided in 1970 to support the organizational activities of the Section on Pediatric Pharmacology of the American Academy of Pediatrics at the annual meeting of the Academy.

Research Grants

An important Foundation activity is support of fundamental research in drug toxicology. Since 1966 a total of 23 research grants have been made for this purpose. Support has terminated on four of these. The remaining 19 grants continue through various periods of time through 1972.

In 1970, new grants were made to the University of Illinois at the Medical Center in Chicago; University of Minnesota School of Medicine; Rochester University School of Medicine; University of Oregon Dental School; Temple University; State University of New York in Buffalo; The University of Texas Medical Center in Dallas; and Stanford University Medical Center.

Eleven grants current in 1969 continued into 1970. These are: The University of Colorado Medical Center, Division of Dermatology, Denver, Colorado; Rutgers University, College of Pharmacy, Newark, New Jersey; Georgetown University School of Medicine-School of Dentistry, Department of Pharmacology, Washington, D.C.; Georgetown University, Renal and Electrolyte Division, Washington, D.C.; Albany Medical College of Union University, Institute of Experimental Pathology and Toxicology, Albany, New York; University of Utah, Department of Pediatrics, Salt Lake City, Utah; Children's Hospital Research Foundation, Institute for Developmental Research, Cincinnati, Ohio; University of Montreal, Department of Pharmacology, Montreal, Quebec, Canada; University of Chicago, Department of Obstetrics and Gynecology, Chicago, Illinois; Johns Hopkins University, Department of Pediatrics, Baltimore, Maryland; and Universities Associated for Research and Education in Pathology, Washington, D.C.

The 19 current research grants fall into the following categories:

Animal-Human Predictability Studies. A grant of $78,654 over a two-year period beginning January 20, 1969, to the Department of Obstetrics and Gynecology, Chicago Lying-In Hospital, Pritzker School of Medicine, University of Chicago, entered its second year in 1970. The principal investigator is Anthony P. Amarose, Ph.D., Assistant Professor, Department of Obstetrics and Gynecology, and the co-investigator is Charles R. Schuster, Ph.D., Associate Professor of Psychiatry, Department of Psychiatry. This work is intended to determine whether a relationship exists between chromosome damage and drug intake. Chromosomes, the threadlike structures in the nucleus of a cell, carry the hereditary elements that enable human beings to reproduce. The study measures the response in the chromosomes of lymphocytes (a form of the white blood cell) and bone marrow cells to drug stimuli.

Many drugs administered during in vitro studies demonstrate chromosome damage. The basic question, however, is whether these drugs will produce
Metaphase spread of rabbit lymphocyte seven days after a single injection at the lethal-dose-zero amount of Mitomycin-C, the positive control drug for the study. The two arrows indicate translocated portions of five chromosomes reducing the normal chromosome number of 44 to 39. 1500X

in vivo the same damage after therapeutic dosages. The in vivo studies with animals consist of as close an in vivo comparison of drug effects as possible to both validate the animal system and evaluate results reported in the chromosome studies of man.

Human volunteers in the study are former drug addicts who have been using opiates, psychedelics, amphetamines, or barbiturates. The research team is studying various parameters, the most important of which is the chromosomology of the volunteers' bone marrow and peripheral blood. The ultimate target would focus on human germ cells, but because of the present impossibility of studying such cells at will, a related cell replenishment system, namely the hematopoietic system, is being utilized. Substantial portions of the work have been completed and submitted for publication.

A grant of $26,000 for a two-year period beginning September 1, 1968, made to Gabriel L. Plaa, Ph.D., Professor and Chairman, Department of Pharmacology, School of Medicine, University of Montreal, ended in 1970. The grant supported a number of studies dealing with the production of intrahepatic cholestasis, a reaction characterized by the development of jaundice and changes in the liver function which can occur in susceptible individuals following treatment with certain drugs.

The overall goal of the effort was to develop an experimental animal system which can be employed to detect intrahepatic cholestasis in the investigational stage of drug development. The protocol called for changes in liver function to be correlated with changes in the liver structure in four species of animals—the rat, mouse, golden hamster, and dog. The parameters used to assess the hepatic dysfunction in the preliminary experiments have included: elevation of serum, bilirubin, serum glutamic-pyruvic transaminase (SGPT) or serum alkaline phosphatase (SAP) and changes in bile flow.

The investigators established a long acting (days) state of cholestasis and a short-acting (hours) cholestasis. A paper on the long acting state of cholestasis has been accepted for publication in Toxicology and Applied Pharmacology. A manuscript of the short-acting cholestasis has been prepared and submitted for publication.

A grant of $15,000 for one year beginning July 1, 1971, was made to Henry L. Price, M.D., Professor of Anesthesiology, Hahnemann College, to support research into the state of circulatory depression which attends the administration of most anesthetics. Specifically, it has been found that certain anesthetics cause an activation of receptors in the heart itself which are capable of restoring circulatory function to or toward normal as anesthesia progresses.

The intended research will attempt to discover an animal model suitable for the study of this phenomenon of “recovery” from or “tolerance” to an anesthetic while it is still being given. By use of the animal model, it is then proposed to learn the mode of action involved whereby anesthetics can act to produce
antagonism to their own depressant actions on the heart. Studies would also be carried out in man.

**Clinical Pharmacology.** A grant of $51,850 for two years beginning July 1, 1970, was made to William T. Beaver, M.D., Associate Professor of Pharmacology, Department of Pharmacology, Georgetown University School of Medicine and Dentistry, to establish a facility for studying the comparative effects of drugs on subjective responses.

The investigation primarily is concerned with the evaluation in patients of drugs whose major effect is in the treatment of symptoms such as pain, anxiety, insomnia and nausea. The initial studies are directed towards the evaluation of potent analgesics in patients with postoperative pain.

During the first months of the study, two problems were examined which are inherent in commonly used techniques for the study of the potency of drugs in postoperative pain: (1) a high drop-out rate in crossover studies due to a decrease in pain intensity before all four treatments in a graded-dose comparison can be made; and (2) undue prolongation of the study and inefficient use of available patients due to initial uncertainty as to the dose level of the test drug. Data collected so far appear to support the feasibility of an alternative method which may overcome these two problems.

A grant of $15,000 for one year beginning July 1, 1970, was made to Louis Lasagna, M.D., Professor of Pharmacology, University of Rochester School of Medicine, for research into gastric physiology and metabolism in affecting the fate of a series of compounds. The long-prevalent notion that the stomach acts primarily as a barrier to passive diffusion of drugs into the circulation will be studied. It is hoped that the examination of a series of compounds in both animals and man, with attention paid to such factors as metabolism by the gastric mucosa, gastric emptying, gastric pH, etc., will add information on the ways in which these factors influence the therapeutic and toxic effects of drugs in man.

A grant of $17,042 for one year beginning June 1, 1970, was made to Donald B. Hunninghake, M.D., Assistant Professor of Medicine and Pharmacology, Department of Pharmacology, University of Minnesota Medical School, to support a project primarily designed to evaluate the utility of plasma drug levels as a guide to more effective therapy. Considerable individual variation in response to a given drug regimen exists. Variation in absorption, excretion and metabolism of drugs as well as drug-induced and disease-induced alterations in these parameters account for many of these different responses. In many cases, the pharmacological or biological response to a drug is related directly to the tissue or plasma concentration of the drug, but relatively fixed-dosage schedules are employed with many drugs. In this study, individual titration of dose and dosage schedules for patients will be done on the basis of plasma level of drugs. The effects of this individual titration on both efficacy and toxicity will be evaluated.

A grant of $30,000 over a two-year period, beginning March 1, 1971, was made...
to John J. Miller, III, M.D., Ph.D., Assistant Professor of Pediatrics, Department of Pediatrics, Stanford University School of Medicine for a study of the relation of drugs to the lupus syndrome. The purpose of the research is to define the way in which certain drugs induce formation of anti-nuclear factors, a group of abnormal antibodies, and to define the relation between these drugs and the spontaneously occurring disease, systemic lupus erythematosus. Systemic lupus is associated with the presence of abnormal antibodies which react with cell nuclei. One of these antinuclear factors, an antibody reacting with deoxyribonucleic acid, probably has a pathogenic role in causing the disease.

The specific purpose of the work is to discover which drugs are most likely to cause antinuclear factors to appear in children and to determine how many children develop antinuclear factors and the associated disease.

Dialyzable Drugs. A grant of $20,000 a year for up to five years, for a total of $100,000, beginning January 1, 1967, to the Renal and Electrolyte Division, Georgetown University Hospital, completed its fourth year during 1970. George E. Schreiner, M.D., Professor of Medicine and Director, Renal and Electrolyte Division, is the principal investigator. These funds have been used to support research related to the hemodialysis of drugs and poisons and to produce an annual registry of dialyzable drugs in cooperation with the American Society of Artificial Internal Organs. Hemodialysis is the removal of certain elements (in this case, drugs) from the blood by the diffusion through a semi-permeable membrane. The artificial kidney uses this procedure.

In 1970, the research group prepared and published, as it had the previous three years, a review of dialyzable drugs and poisons. This appeared in the 1970 TRANSACTIONS of the American Society of Artificial Internal Organs.

The grant has also enabled the Renal and Electrolyte Division to maintain the capability of studying new drug-overdose cases as they arrive on the clinical service. Data obtained in this way is obtainable through no other form since it is not permissible to give drugs in such a level in human research.

Drug-Related Structural Studies. A grant of $25,000 a year for a four-year period totaling $100,000, which began August 1, 1967, to the Institute of Experimental Pathology and Toxicology of the Albany Medical College of Union University, Albany, New York, entered its final year in 1970. The principal investigator is Frederick Coulston, Ph.D., Director of the Institute. Funds during the first three and a half years have accelerated the Institute’s studies of the relation of structural changes in the subcellular organelles of important tissues to the actions of chemicals and drugs. This program has as its purpose the establishment of selected critical areas of experimentation in animals with the anticipation that a valid prediction of safety can be made in man with limited, but precise investigation.

Drug Surveillance. A grant of $20,543 made to the Universities Associated for Research and Education in Pathology for support during 1969-1970 of the Registry
Dr. Ernest F. Zimmerman (third from left) with his research group is exploring the elevation of fetal palates by polarization microscopy, and the effects of glucocorticoids on this process. Also seen are Miss Donna Bowen, Dr. David Gustine and Dr. Floyd Andrew.

of Tissue Reactions to Drugs, Armed Forces Institute of Pathology, ended in June, 1970. The Registry has been co-sponsored and equally supported by the American Medical Association, the Food and Drug Administration, the National Institutes of Health, and the Foundation. Nelson S. Irey, M.D., is the Registrar.

The Registry obtains biopsy and autopsy tissue specimens on a voluntary reporting basis from participating pathologists. The Registry subjects the specimens to microscopic examination and reports its findings to the referring pathologist. As of June 1970, the Registry had accessioned approximately 1,500 cases in its active files. Over 9,000 cases continued to be available to the Registry in its reserve file.

A set of educational publications which have been produced by the Registry entitled “Diagnostic Problems and Methods in Drug-Induced Diseases”, are available to medical schools along with a set of lantern slides.

**Fetal-Neonatal Pharmacology.** An award of $54,000 for three years to the Department of Pediatrics, University of Utah and Alan K. Done, M.D., Professor of Pediatrics, was concluded in 1970. This was for a study of the drug potentiation of kernicterus, a condition of hyperbilirubinemia associated with jaundice which may produce brain damage in the newborn.

During the three years of the grant, the research team found that many of the *in vitro* procedures which have been used to measure the ability of drugs to compete with bilirubin for protein-binding were unreliable and were not consistent with the findings in the Gunn rat, which has an inherited inability to conjugate bilirubin. The research team has found that the procedures of bilirubin ultrafiltration, measurements of dye-binding capacity and kinetic measurements of binding offer the greatest promise among the *in vitro* techniques for determining drug inhibition of bilirubin-albumin binding.

A grant of $50,000 a year for five years for a total of $250,000 made in 1967 to Josef Warkany, M.D., Professor of Research Pediatrics, on behalf of the Children’s Hospital Research Foundation for partial support of the activities of the Division of Fetal Pharmacology of the Institute of Developmental Research entered its fourth year in 1970. The Institute, which opened in June 1968, has used Foundation support primarily in the Division of Fetal Pharmacology to support staff and purchase the equipment needed for the basic research within this unit. Ernest F. Zimmerman, Ph.D., is the Director of the Division.

Dr. Zimmerman has become interested in the molecular mechanisms by which glucocorticoids induce cleft palate in mice. One recurring finding in teratology is that the most sensitive period of administration of a teratogen is several days before the morphologic appearance of the organ which is ultimately transformed. It has been shown that there is a sequential synthesis of different messenger RNA (mRNA) molecules during development. This results in translation of proteins at later times. A tentative posulate put forth by Dr. Zimmerman is that such
Dr. Paul S. Leitman, with the technical assistance of Mrs. Elizabeth Moen, is involved in the study of some effects of antibiotics on mammalian cell mitochondrial protein synthesis.

an inhibition of mRNA synthesis early in development by the glucocorticoid triamcinolone leads to a later inhibition of protein synthesis and thus congenital malformation.

Dr. Robert E. Ganschow, an associate of Dr. Zimmerman's has been interested in the control of gene expression in developing and mature animal systems. He has been supported through the Foundation grant in his investigations of the genetic control mechanisms which determine the biosynthesis, movement, compartmentalization and degradation of enzymes in animal cells, using inbred strains of mice which show heritable enzyme variations.

A grant of $50,000 over a two-year period beginning January 1, 1969, to Robert E. Cooke, M.D., Given Foundation Professor of Pediatrics, Johns Hopkins University School of Medicine ended in 1970. This was for the basic and clinical research on the effects of drugs given to the developing organism. The grant supported efforts in a new unit devoted to developmental pharmacology within the Department of Pediatrics under the direction of Paul S. Leitman, M.D. Emphasis in the laboratory is on the pharmacologic agents affecting protein synthesis and its regulation. Much of the effort has been directed toward the effects of antibiotics on mitochondrial protein synthesis. Several studies were conducted with respect to inhibitors of RNA polymerase (rifampicin), translocation in protein biosynthesis (fusidic acid), peptide bond formation (chloramphenicol) and several analogs of emetine. In general, the aim of the grant to assist in establishing a pediatric pharmacology unit has been met.

A grant of $30,000 over a two-year period, to begin February 1971 was made to Charles E. Mize, M.D., Ph.D., Assistant Professor of Pediatrics, The University of Texas Southwestern Medical School at Dallas for a study of selective mechanisms of antibiotic toxicity in children. The co-investigator is Howard G. Worthen, M.D., Ph.D., Professor of Pediatrics. The study will concentrate on the effects of certain antibiotics on selected new membrane formation essential to cell growth in renal tissue of rabbits. The response to various selected antibiotics, will be investigated with radioactive tracer experiments, electron microscopic determination of anatomic changes and the enzymatic and chemical studies of the membranes.

A grant of $14,450 for one year beginning May 15, 1970, was made to Walter L. Gabler, D.D.S., Ph.D., Associate Professor, Division of Oral Biology and Department of Biochemistry, University of Oregon Dental School, to study drug metabolism during pregnancy. To examine the problem, an antiepileptic drug will be tested on pregnant and non-pregnant Rhesus monkeys to determine if pregnancy alters the normal metabolism of an anticonvulsant drug. A reduction in metabolism of drugs during pregnancy can have significant pharmacological implications for both the mother and fetus, particularly if the drug is capable of interfering with protein synthesis.
A grant of $58,000 over a two-year period beginning May 1, 1970, was made to Richard E. Behrman, M.D., Professor of Pediatrics, Department of Pediatrics, University of Illinois at the Medical Center (Chicago) for studies to characterize the pharmacologic effect of phenobarbital on fetal and newborn monkeys by evaluating the effects on blood pressure, heart rate, ECG, cardiac output, oxygen consumption and organ blood flows. The kinetics of the placental transfer will be studied as well as the effects on the fetal and placental circulations, particularly the liver and brain. The investigations will attempt to compare the dose response relationships of the effects of phenobarbital on increasing bilirubin conjugating activity and protecting the brain from asphyxia before and after birth to the dose response relationships for inducing fetal and newborn depression and hypotension. The observations are significant in increasing the understanding and the ability to evaluate the in utero and neonatal treatment of human infants with phenobarbital.

**Nutritional Deficiencies-Drug Action.** A grant of $29,459 over a two-year period to Christina VanderWende, Ph.D., Professor of Biochemistry and Pharmacology, Rutgers University, entered its second year in 1970. The funds provide support for studies of the interaction of vitamin deficiencies and drug action. The extension of these studies will eventually include studies of protein deficiencies and a generalized malnutrition state on drug action and drug toxicity. Preliminary studies have shown that in mice fed a thiamine deficient diet for one week, the sleeping time after phenobarbital is increased three to fourfold. If the deficiency is allowed to continue for three weeks, a dose which proved to be safe for control animals, killed all of the deficient animals. These studies, in a preliminary fashion, make it apparent that both the pharmacologic activity and the toxicity of drugs can be markedly influenced in deficiency states. These, and other findings relative to thiamine deficiency, are being prepared for publication. The ultimate objective of the project, therefore, is to systematically determine what kind of deficiencies can alter drug actions and which classes of drugs are most likely to be altered.

The investigators will use widely prescribed drugs such as barbiturates and tranquilizers and over-the-counter items, such as aspirin. The study will also include amphetamines and narcotics (morphine) because of their wide-involvement in drug abuse. The deficiency states to be studied in rats will be those involving the B vitamins, and vitamins A, E, K and C.

A grant of $44,590 over a two-year period, to begin April 15, 1971, was made to Sumner A. Yaffe, M.D., Professor Pediatrics, Department of Pediatrics, State University of New York at Buffalo, to study the effect that malnutrition may have on the activity of hepatic drug-metabolizing enzymes. Both acute and long-term effects of nutritional deficiency will be studied. Drug metabolism is the most
significant determinant of the duration of drug action in the organism. Elucida-
tion of the effects that nutritional status has on drug metabolism under controlled
experimental situations will permit correlation with human malnutrition situations.
Animal studies also permit clarification of the basic molecular mechanisms which
may be responsible for overall alteration in drug metabolism as a result of
nutritional deficiency. The data obtained in these animal studies should give
some understanding of the changes anticipated in drug metabolism in infants
and children and are a necessary prerequisite to clinical studies.

Photoactive Compounds. A grant of $14,500 for one year, beginning July 1,
1969, made to the University of Colorado Medical Center for support of a study
of the possible beneficial effects of light on drugs, ended in 1970. The research
is under the direction of Guinter Kahn, M.D., Assistant Professor of Dermatology.
The study is of the changes which occur when drugs are exposed to various
wave lengths of radiation.

While the study focused on drugs which can harness the energy of long-wave
ultraviolet light to cause useful anti-cellular effects, the research also attempted
to determine if these photosensitizing drugs can enhance the effect of X-ray
radiation on any part of the cell. Work was also accomplished on finding new
depigmenting agents. Depigmentation of this type was reported in the Archives
of Dermatology, in August 1970. This research won first prize in the Hollis Garrard
Memorial Essay Contest of the North American Dermatologic Society.

Publications

A grant of up to $18,500 was authorized in 1969 for the preparation of the book
entitled "The Fundamentals of Drug Metabolism and Disposition." The contents
of this book are being drawn from the presentations at three workshops on
drug metabolism supported by the PMA Foundation in 1966, 1967 and 1968.
Wider availability of the information presented at these workshops was con-
sidered highly desirable, since the meetings were limited to 40 participants
each. The editors of the book are the directors of the workshops, Drs. Bert N.
La Du, New York University; H. George Mandel, George Washington University;
and E. Leong Way, University of California, San Francisco. The contributing
authors in most instances are the members of the faculties at the three workshops.
The Foundation is cooperating with the Drug Research Board, National Academy
of Sciences-National Research Council in the effort. The estimated publication
date is Spring 1971.

A grant of up to $22,000 was made in 1969 to the American Society for Pharma-
cology and Experimental Pharmacology and Experimental Therapeutics for sup-
port of the preparation and publication of a recruitment brochure for the field
of pharmacology. Over the past several years, the American Society of Pharma-
Clinical Pharmacology

More than one

Pharmacology-Morphology


cology and Experimental Therapeutics had distributed nearly 450,000 copies of a brochure entitled “A Career in Pharmacology,” written for the high school and beginning college student. The new brochure, prepared to reflect the changes occurring in the sciences over the past ten years, is aimed at a somewhat more advanced student. About 200,000 copies were published in 1970.

A grant of $12,000 beginning in 1971 was made to Ruth R. Levine, Ph.D., Professor of Pharmacology, Boston University School of Medicine, to assist in the preparation of a textbook on the principles of pharmacology for use at the undergraduate level in the general curriculum of a college. The purpose of this textbook is to provide a concise source of the kind of pharmacologic knowledge that would be useful to anyone wishing to understand the ways in which chemicals interact with living organisms. It is being written primarily for the non-professional to provide the opportunity to acquire and share with the professional the basic information that will help the non-professional cope with a society where the use of drugs is constantly increasing and where exposure to chemicals can hardly be avoided.

The emphasis in the book will be placed on the basic concepts and principles which are fundamental to understanding the action of drugs at any level of complexity. The biochemical and physiologic concepts needed to understand the pharmacologic principles will be an integral part of the text. Readers of diverse backgrounds need have in common only a working knowledge of general chemistry and biology. Hopefully, the availability of a textbook will serve the further purpose of implementing the presentation of courses in pharmacology in non-professional schools as part of a liberal arts curriculum.

Education and Training Programs

To further its objectives in the field of education, the Foundation sponsors two programs in clinical pharmacology and one in the combined fields of pharmacology and morphology. The two clinical pharmacology programs have provided educational opportunities for a number of individuals at both the student and the faculty level.

Clinical Pharmacology. Through the “Faculty Development Awards in Clinical Pharmacology” program, the Foundation makes two-year awards to medical schools for salary support of full-time junior faculty members. The level of support is variable but in keeping within the existing salary structure of the applicant university. The Board of Directors has established a yearly fund of $100,000 for this program.

With the awards made in 1970 and scheduled to begin July 1, 1971, 19 individuals have now been supported under this program since its inception in 1967. While the award is for a two-year period, a third year of support is available to those
awardees who, at the end of their first year, show sufficient need for the third year. An additional fund of $50,000 has been authorized to provide for the contingency of requests for a third year of support.

Recipients of new faculty awards, which begin July 1, 1971, are:

- I. David Goldman, M.D., Assistant Professor of Medicine and Pharmacology, University of North Carolina School of Medicine. Dr. Goldman will undertake studies of the mechanisms which facilitate drug-cell interactions. He will also continue his teaching responsibilities with fourth year medical students in special seminars in computer methods, transport mechanisms and statistical methods.

- Urs A. Meyer, M.D., Instructor of Medicine, Department of Medicine, University of California, San Francisco Medical Center. Dr. Meyer's primary research interest will be in the area of drug metabolism, with the goal of developing an in vitro model of drug-induced increase in synthesis of P450 enzymes using cell culture techniques. He will have teaching responsibilities on morning rounds and will participate in the clinical pharmacology conferences, both as commentator and primary lecturer as well as leading some subspecialty pharmacology sessions in various clinical departments.

- Alan S. Nies, M.D., Assistant Professor of Medicine and Pharmacology, Vanderbilt University, School of Medicine. Dr. Nies will extend his research interests through the study of the effects of alterations of regional blood flow by disease or drugs. He will play a leading role in conferences in clinical pharmacology for house staff and in teaching senior medical students.

- Harold C. Strauss, M.D., Associate in Pharmacology, College of Physicians and Surgeons, Columbia University. Dr. Strauss will continue his studies designed to improve understanding of antiarrhythmic drug actions. He will also have teaching responsibilities in the Department of Pharmacology and in the instructional program of the Cardiac Intensive Care Unit.

- Wilmer Leigh Thompson, M.D., Ph.D., Assistant Professor of Medicine and Assistant Professor of Pharmacology and Experimental Therapeutics, Johns Hopkins Hospital. The award will enable Dr. Thompson to do research on drug therapy in seriously-ill patients. He will also be involved in teaching clinical pharmacology to students in the last three years of medical school.

- Thomas Whitsett, M.D., Assistant Professor of Medicine and Pharmacology and Acting Associate Director of the Clinical Pharmacology Division of the University of Oklahoma Medical Center. Dr. Whitsett will study cardiovascular and renal effects of autonomic and antihypertensive agents. His responsibilities will also include an active teaching program directed toward house staff, senior and sophomore medical students.
Recipients of the awards which began July 1, 1967, are:

- Faruk S. Abuzzahab, Sr., M.D., Ph.D., Assistant Professor, Department of Psychiatry and Pharmacology, University of Minnesota, is conducting research in both basic and clinical pharmacology.
- John S. Holcenberg, M.D., Assistant Professor, Division of Clinical Pharmacology, Department of Medicine, University of Washington, Seattle, is extending his training in biochemical approaches to clinical pharmacology.
- John L. McNay, M.D., Associate Professor of Medicine and Assistant Professor of Pharmacology, Emory University, is conducting research in renal physiology and pharmacology.

Recipients of awards which began July 1, 1968, and which were extended until June 30, 1971, are:

- William Y. W. Au, M.D., Assistant Professor of Pharmacology and Medicine, University of Rochester, is engaged in research on the effects of hormones and other agents affecting bone metabolism.
- Arthur H. Hayes, M.D., Assistant Professor, Pharmacology and Medicine, Cornell University, is furthering his training in the cardiovascular field.
- Donald S. Robinson, M.D., Assistant Professor of Medicine and Pharmacology, University of Vermont, is involved in studies in biochemical pharmacology.

Recipients of awards which began July 1, 1969, are:

- Vincent S. Aoki, M.D., Assistant Professor, Department of Internal Medicine and Pharmacology, University of Iowa, is involved in studies of the effects of drugs on the pulmonary vascular bed. He was awarded a third year of support extending until June 30, 1972.
- Lester F. Soyka, M.D., Associate Professor of Pediatrics, Department of Pediatrics, University of Illinois Medical Center in Chicago, is involved in research dealing with immaturity at the biochemical level and other developmental studies.
- Pate D. Thomson, M.D., and Instructor, Department of Medicine, University of California, San Francisco Medical Center when the award was made, resigned the second year of the award to take a position of chief of a cardiac unit in a California hospital.
- Stanley C. Ushinski, M.D., an Assistant Professor of Pediatrics and Pharmacology, University of Pittsburgh, when the award was made, resigned the second year of the award to enter private practice.

Recipients of the awards which began July 1, 1970, are:

- Arthur J. Atkinson, M.D., Assistant Professor of Medicine, Department of Medicine, Northwestern University Medical School, is conducting research into cardiac drugs in relation to their effectiveness.
- Samuel A. Cucinell, M.D., Assistant Professor of Medicine, Emory University School of Medicine is extending his research efforts on drug metabolism in man.
Dr. Arthur Hayes, left, a faculty development awardee discussing a clinical problem with Mr. Kenneth Blanchard, recipient of a medical student traineeship award, both of Cornell University College of Medicine.

Geographical distribution of Foundation awards under the "Medical Student Traineeships in Clinical Pharmacology" program, 1967-1970.

Aryeh Hurwitz, M.D., Assistant Professor of Medicine and Pharmacology, Clinical Pharmacology-Toxicology Center, University of Kansas Medical Center, is conducting research into the mechanism of action of compounds which are poisonous to liver cells.

The "Medical Student Traineeships in Clinical Pharmacology" offered for the first time in 1966, provide opportunities to medical students to become aware of the basic techniques used in the field of clinical pharmacology. Hopefully, these students will sustain their interests in clinical pharmacology and choose this field as a career. This program provides a stipend of $1,000 to each student for a three-month period. A yearly fund of $20,000 has been authorized for this program. Since 1967, when the first awards were made, 80 awards have been made to medical schools across the United States.

The universities and students receiving awards in 1970 are:

University of California, Irvine
    Stephen C. Spreiter

University of California, San Diego
    Jeffery N. Wilkins

University of Colorado
    John R. Heckenlively

Cornell University Medical College
    Kenneth R. Blanchard; Ph.D.

Cornell University Medical College
    Kenneth V. Schwartz

Georgetown University
    Joseph R. McClellan
    William Tamborlane, Jr.

Johns Hopkins University
    Marc C. Hochberg

Howard University
    Nicholas A. Ongele

Louisiana State University
    Charles R. Pearson

Marquette School of Medicine
    William H. Hass

University of Miami
    Brian G. Schuster

University of Minnesota
    Gerald E. Merwin

University of Oklahoma
    John M. Kessinger

University of Pennsylvania
    Nicholas H. Dienel

University of Pennsylvania
    Philip Harber

University of Rochester
    Stephen J. Gorton

University of Southern California
    Joseph C. Anderson

Vanderbilt University
    David H. Robertson

Yale University
    Robert J. DeLorenzo
Pharmacology-Morphology. A postdoctoral program offered by the Foundation is the PMA Foundation Fellowship Awards in Pharmacology-Morphology. Recent developments indicate the need for studies of drug-evoked changes in structure and their functional significance. The program was initially offered in 1967 with the aim of advancing understanding of drug action through discovery of specifically related cellular and tissue changes; and, concurrently, to uncover associations between normal and abnormal function in particular tissues and cellular structure.

The awards are for two years each and, in exceptional circumstances, may be extended for an additional year. The level of support is variable and is aimed at keeping within the existing stipend levels for similarly trained individuals within the applicant university. During the three years of the program, 10 awards have been made.

The fellowship program is designed to support individuals trained to study the actions of drugs in relation to morphologic approaches (cytology, histology, ultrastructure, pathology). This pursuit applies an interdisciplinary training. Although the program requires that a candidate be qualified primarily either in a morphologic specialty or in pharmacology, training in the complementary discipline need not be formal. The aim is to have the candidate gain familiarity with a new disciplinary approach by using his primary discipline as a medium for acquiring the second. A yearly fund of $70,000 has been set aside for this program.

Recipients of the awards which began July 1, 1970, are:

- Carole Davis Kimmel, Ph.D., Division of Toxicology, Kettering Laboratory, Department of Environmental Health, College of Medicine, University of Cincinnati. Dr. Kimmel will study the effects of betapropiolactone on the rabbit embryo and fetus to determine how this agent binds to DNA, RNA protein and other subcellular components, and any teratogenic or carcinogenic relationships.
- Patricia J. Bingham, D.Phil., Department of Pharmacology and Toxicology, University of Rochester. Dr. Bingham will use autoradiography techniques to study the mechanism of action and localization of hormones and other agents which affect bone formation and resorption.
- Roy J. Baerwald, Ph.D., Department of Medicine, University of Miami. Dr. Baerwald will investigate structural changes induced by such drugs as colchicine, vinblastine and vincristine in a range of invertebrate and vertebrate cells.
- Richard F. Hoyt, Ph.D., Department of Pharmacology, Harvard School of Dental Medicine. He will study the relationship between hormone and drug-induced changes in subcellular structure, particularly three strains of cultured mammalian tumor cells.
Robert E. Seegmiller, Ph.D., Department of Molecular, Cellular and Developmental Biology, University of Colorado. Dr. Seegmiller will study in mice the genetic-environmental interactions which influence the differentiation of cartilage and, subsequently, the morphology of limbs.

Recipients of awards which began July 1, 1968, are:

- David W. Hiott, Ph.D., Department of Pharmacology, Medical College of South Carolina. He gained additional experience with the procedures of audioradiography and in certain techniques and interpretations of histochemistry, particularly at the electron microscopic level. His research efforts are directed toward the investigation of ultrastructural changes in the canine and hamster cardiac muscles by quinidine and daunomycin.
- John O. Lindower, M.D., Ph.D., Department of Pharmacology, The Ohio State University. Dr. Lindower is engaged in studies of the effect of digitalis by correlating the changes the compound produces in heart cells. Isolated small animal hearts are perfused with the digitalis medium while a recording device measures the more forceful contraction that the drug produces in the heart. After the drug effect has been demonstrated, small samples of the heart muscle are examined by the electron microscope to detect any changes that have been produced by the drug.
- Timothy J. Mathew, M.B., B.S., Renal and Electrolyte Division, Georgetown University Hospital. He was engaged in studies directed to examination of platlets in the pathogenesis of transplant rejections. An attempt was made to alter histologic pattern rejection by using drugs directed at changing the platlet function. Following the conclusion of the fellowship, Dr. Mathew returned to Australia to assume responsibilities as Assistant Director, Renal Unit, Royal Melbourne Hospital.

Recipients of the awards which began July 1, 1969, are:

- Andrew K. S. Ho, Ph.D., Department of Pharmacology, University of California, San Francisco Medical Center. Dr. Ho is extending his training through studies of the effect of cell structure and tissue function of the various psychopharmacologic drugs by a combination of techniques of electron microscopy, histochemistry and biochemical pharmacology. The findings are correlated to the therapeutic use of these drugs and their effect on behavior.
- William J. Scott, Jr., D.V.M., Ph.D., Children's Hospital Research Foundation, Cincinnati, Ohio. The award is enabling Dr. Scott to advance his training through a series of studies in rats and primates of the teratogenicity of a group of carbonic anhydrase inhibitors. He is attempting to determine the mechanism of teratogenetic action.
Contributions are accepted from corporate and individual sources. The Foundation does not accept contributions which are so restricted as to place their use outside the policies of the Foundation. Contributions to the Foundation are deductible for Federal income tax purposes.

The Board of Directors of the Foundation decided at the outset that, as a minimum, annual contributions of $500,000 would be sought for each of the first three years of the Foundation’s activities, extending through 1968, with larger amounts anticipated thereafter. In requests for voluntary support to PMA Member Firms, a guideline is suggested. Each firm is asked to consider a contribution equal to .015% of its domestic and international pharmaceutical sales.

**Income.** The total income in 1970 was $696,904. Of this amount $619,714 came from contributions. The balance of $77,190 came from investments and refunds on unexpended balances on grants. The 1970 contributions represent an increase of approximately 5.5% over the $587,220 received in 1969, a 9.1% increase over the $567,951 received in 1968, a 14% increase over the $543,392 received in 1967 and a 23% increase on the $503,297 received during the Foundation’s first contribution period covering 1965-1966.

Contributions were received from approximately three of every four PMA Member Firms. About one half of the PMA Associates also joined in supporting the Foundation. Contributions were also received during 1970 from several individuals and groups in the health field.

**Expenditures.** Grants, Foundation-sponsored programs and administrative expenses for 1970 amounted to $647,163. Of this amount $572,578 represented expenditures for grants and Foundation-sponsored programs. There was a fund balance of $807,645 as of December 31, 1970. This figure, however, does not reflect the tentatively authorized, undisbursed amounts for some of the grants and programs described earlier. The Foundation reports these amounts as expenditures when the funds are distributed. As of December 31, 1970, this contingency liability totaled $887,974. Some of these grants represent amounts to be paid over the next two years. Part of this liability will be met from anticipated income in 1971 and succeeding years. During 1971 the estimated amount to be paid on this tentative commitment is $455,000.

**Financial Reports.** The Foundation’s financial position as of December 31, 1970 has been audited by the accounting firm of Ernst and Ernst. Copies of this statement will be supplied upon request.

Financial statements have been issued to contributors quarterly during 1970. These reports are prepared by the Washington, D.C. accounting firm of Buchanan and Company. Quarterly reports will continue to be distributed to the Foundation’s contributors during 1971.

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### Contribution Income 1965-1970

<table>
<thead>
<tr>
<th>Year</th>
<th>Income (Thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965</td>
<td>$625</td>
</tr>
<tr>
<td>1966</td>
<td>~600</td>
</tr>
<tr>
<td>1967</td>
<td>~550</td>
</tr>
<tr>
<td>1968</td>
<td>~525</td>
</tr>
<tr>
<td>1969</td>
<td>~500</td>
</tr>
<tr>
<td>1970</td>
<td>~475</td>
</tr>
</tbody>
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![Graph showing contribution income from 1965 to 1970]
# Statement of Income and Expenditures

For the year ended December 31, 1970

<table>
<thead>
<tr>
<th>Income</th>
<th>Amount</th>
</tr>
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<tbody>
<tr>
<td>Contributions—Note a</td>
<td>$619,714</td>
</tr>
<tr>
<td>Income from Investments</td>
<td>68,639</td>
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<tr>
<td>Miscellaneous Income</td>
<td>8,551</td>
</tr>
<tr>
<td><strong>TOTAL INCOME</strong></td>
<td><strong>$696,904</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Expenditures</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Grants—Note b</td>
<td></td>
</tr>
<tr>
<td>American Academy of Pediatrics</td>
<td>$1,000</td>
</tr>
<tr>
<td>American Society of Pharmacology and Experimental Therapeutics</td>
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</tr>
<tr>
<td>Recruitment Brochure in Pharmacology</td>
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<tr>
<td>Supplemental Training</td>
<td>30,373</td>
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<tr>
<td>Workshop</td>
<td>18,645</td>
</tr>
<tr>
<td>Children's Hospital Research Foundation</td>
<td>50,000</td>
</tr>
<tr>
<td>Clinical Pharmacology Faculty Program</td>
<td>175,011</td>
</tr>
<tr>
<td>Georgetown University School of Medicine</td>
<td>12,000</td>
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<tr>
<td>Georgetown—Kidney Fund</td>
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</tr>
<tr>
<td>Institute of Experimental Pathology and Toxicology</td>
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</tr>
<tr>
<td>Johns Hopkins University</td>
<td>25,000</td>
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<tr>
<td>Medical Student Traineeships in Clinical Pharmacology</td>
<td>20,000</td>
</tr>
<tr>
<td>National Academy of Sciences</td>
<td>6,000</td>
</tr>
<tr>
<td>Pharmacology-Morphology Program</td>
<td>59,000</td>
</tr>
<tr>
<td>Regents of the University of California</td>
<td>2,000</td>
</tr>
<tr>
<td>Rutgers University</td>
<td>14,318</td>
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<tr>
<td>University of Chicago</td>
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<tr>
<td>University of Illinois Medical Center</td>
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<tr>
<td>University of Minnesota</td>
<td>17,042</td>
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<tr>
<td>University of Oregon Dental School</td>
<td>14,450</td>
</tr>
<tr>
<td>University of Rochester</td>
<td>15,000</td>
</tr>
<tr>
<td><strong>Administrative expenses</strong></td>
<td><strong>$572,578</strong></td>
</tr>
<tr>
<td><strong>Total expenditures</strong></td>
<td><strong>$647,163</strong></td>
</tr>
<tr>
<td><strong>Excess of income over expenditures</strong></td>
<td><strong>$49,741</strong></td>
</tr>
<tr>
<td><strong>Fund balance at January 1, 1970</strong></td>
<td><strong>$757,904</strong></td>
</tr>
<tr>
<td><strong>Fund balance at December 31, 1970</strong></td>
<td><strong>$807,645</strong></td>
</tr>
</tbody>
</table>

Note a—The Foundation received contributions of $53,466 prior to December 31, 1970 which the Foundation considered applicable to 1971 and, therefore, are not recorded as income in 1970.

Note b—The Foundation has committed itself, subject to review, to make certain research grants. At December 31, 1970, the amounts still to be disbursed with respect to these grants aggregated $887,979 of which approximately $455,603 is expected to be disbursed during the year 1971. No liability has been reflected for these amounts at December 31, 1970.
PURPOSE

The PMA Foundation was established to promote the betterment of public health through scientific and medical research, with particular reference to the study and development of the science of therapeutics. In achieving this goal, the Foundation plans and initiates scientific and medical research activities, collects and disseminates the results of these activities, and provides financial support and aid to individuals or institutions whose purposes are scientific, educational or charitable. Certain guidelines have been developed to promote the wise and proper use of the limited resources available. The areas of interest agreed to initially, and which still govern the distribution of funds, are support of fundamental research in drug toxicology, and support of programs of research and training for personnel in clinical pharmacology and drug evaluation.

Throughout the year, programs have been supported and developed which provide the means of achieving the goals of the Foundation. Many worthwhile proposals have been submitted. It has been necessary to limit support to those which hold the highest promise of advancing the purposes of the Foundation.

Those areas not supported within the existing guidelines are:

1) Research on specific drugs. This exclusion is not meant to preclude support of projects which, of necessity, use a number of drugs or a class of drugs to establish a methodology or screening program of potential general applicability. It does exclude those efforts primarily aimed at learning more about specific drugs or classes of drugs.

2) Funds for construction. The Foundation is not unmindful of the needs and the tremendous pressures for private funds for construction projects. However, it is believed that the scientific community can be better served by channeling the Foundation's available resources into other areas.

3) Funds for travel.

4) Funds to cover entertainment costs.

The programs and grants described earlier in this report provide examples of the ways in which the Foundation has interpreted these guidelines.
BEGINNINGS

For those of you who, through this Annual Report, learn of the Pharmaceutical Manufacturers Association Foundation for the first time, a brief resumé of the history which led to its formation is in order.

One event most influential in promoting the establishment of the PMA Foundation was the work and the Final Report of the Commission on Drug Safety, a study group formed by the Pharmaceutical Manufacturers Association in the Fall of 1962. The Commission was charged to make a study of the entire problem of drug safety and to come forth with recommendations. It carried out its work during the time of the urgency of the thalidomide situation. Special attention was given by the Commission initially to drug-induced fetal malformations. It became evident, however, that the most profitable line of inquiry would be to attack the overall problem of drug safety. This Commission of distinguished membership, experts from universities, industry and government, arrived at a series of recommendations.

A continuing theme expressed in a variety of ways by these authorities was that the pharmaceutical industry should show more interest in the conduct of basic studies in drug toxicology, with the suggestion that co-operative sponsorship of such fundamental projects would have the greatest potential for uncovering new information. To make such studies possible, the Commission suggested a number of alternative mechanisms.

One was to establish a foundation. This, as well as many of the Commission's other recommendations, was considered by the PMA Board of Directors for some months following publication of the Commission's report. On May 31, 1965, the PMA announced the establishment of the PMA Foundation. The initial operating funds were supplied by the PMA, and sustaining support for the Foundation has come from voluntary contributions from PMA Member Firms and Associates, industrial concerns, organizations and individuals with an interest in health care research.
The PMA Foundation operates through a Board of Directors and three advisory committees. The Chairman of the Board is H. W. Blades, C. Joseph Stetler is President, Raymond M. Rice, M.D., is Vice President, and Thomas E. Hanrahan is Executive Director. Mr. Blades was elected to the Chairmanship of the Board in April, 1970 following the resignation of Mr. Henry Gadsden. H. Robert Marschalk, President, Richardson-Merrell, Inc., was elected Vice Chairman and Daniel C. Searle, President and Chief Executive Officer, G. D. Searle & Co., was elected Secretary-Treasurer.

At the PMA Annual Meeting in 1970, V. D. Mattia, M.D., President, Hoffmann-La Roche, Inc. and Austin Smith, M.D., Chairman of the Board and President, Parke, Davis & Company, were elected to the Board of Directors of the Foundation to fill the vacancies created by the resignations of Henry W. Gadsden, President, Merck & Co., Inc., and E. Gifford Upjohn, M.D., Member of the Board, The Upjohn Company.

In continuing to seek the most worthwhile activities for support, the Board of Directors has had the advice of extremely knowledgeable individuals, serving on three advisory committees.

The Scientific Advisory Committee has the responsibility of making recommendations to the Board of Directors on all scientific grant requests and on self-initiated scientific undertakings. Irwin C. Winter, Ph.D., M.D., Vice President, Medical Affairs, G. D. Searle & Co., Chicago Illinois, is Chairman of this committee. To increase its effectiveness, the Chairmen of the Medical and the Research and Development Sections of the PMA are invited to serve as ex-officio members of the committee.

The Advisory Committee to the Faculty Development Awards in Clinical Pharmacology program is charged with making recommendations to the Board of Directors on all applications received for these awards, as well as those applications received under the Medical Student Traineeships in Clinical Pharmacology program. The Chairman of this committee until the end of November, 1970 was Thomas C. Chalmers, M.D., Director, Clinical Center and Associate Director, National Institutes of Health, Bethesda, Maryland. John A. Oates, M.D., Professor of Medicine and Pharmacology, Vanderbilt University, School of Medicine, Nashville, Tennessee, was named Chairman to succeed Dr. Chalmers.

The Advisory Committee to the PMA Foundation Fellowship Awards in Pharmacology-Morphology program has the responsibility for making recommendations to the Board of Directors on all applications under this program. The Chairman of this committee is Walter F. Riker Jr., M.D., Chairman, Department of Pharmacology, Cornell University Medical College, New York, New York.
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DANIEL C. SEARLE, Secretary, Treasurer
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RAYMOND M. RICE, M.D., Vice President
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Parke, Davis & Company
Detroit, Michigan

FOSTER B. WHITLOCK, Executive
Committee
Johnson & Johnson
New Brunswick, New Jersey
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Vice President, Medical Affairs
G. D. Searle & Co.
Chicago, Illinois

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Head, Division of Clinical Pharmacology
University of Washington
Seattle, Washington

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Wyeth Laboratories
Philadelphia, Pennsylvania

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Vice President for Research
Hoffmann-La Roche Inc.
Nutley, New Jersey

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Department of Pharmacology
Medical College of Ohio at Toledo
Toledo, Ohio

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Medical Administration
The Lilly Research Laboratories
Eli Lilly and Company
Indianapolis, Indiana

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President, Therapeutics Research Division
Dome Laboratories
West Haven, Connecticut

AMEL R. MENOTTI, Ph.D.
Vice President-Scientific Director
Bristol Laboratories
Syracuse, New York

JAMES M. PRICE, M.D., Ph.D.
Vice President, Experimental Therapy
Abbott Laboratories
North Chicago, Illinois

WALTER F. RIKER, JR., M.D.
Chairman, Department of Pharmacology
Cornell University Medical College
New York, New York

E. LEONG WAY, Ph.D.
Professor of Pharmacology
University of California
San Francisco Medical Center
San Francisco, California

* Resigned, December 30, 1970
Faculty Development Awards in Clinical Pharmacology Advisory Committee

JOHN A. OATES, M.D., Chairman  
Professor of Medicine and Pharmacology  
Vanderbilt University, School of Medicine  
Nashville, Tennessee  

JOHN J. BURNS, Ph.D.  
Vice President for Research  
Hoffmann-La Roche, Inc.  
Nutley, New Jersey  

*THOMAS C. CHALMERS, M.D.  
Director, Clinical Center  
National Institutes of Health  
Bethesda, Maryland  

GLENN W. IRWIN, JR., M.D.  
Dean, School of Medicine  
Indiana University  
Indianapolis, Indiana  

ROBERTS M. REES, M.D.  
Vice President and Director  
Department of Medical Research  
Winthrop Laboratories  
New York, New York  

WALTER F. RIKER, JR., M.D.  
Chairman, Department of Pharmacology  
Cornell University Medical College  
New York, New York  

JOSEPH F. SADUSK, JR., M.D.  
Group Vice President, Medical and Scientific Affairs  
Parke, Davis & Company  
Detroit, Michigan  

ALBERT SJOERDSMA, M.D., Ph.D.  
Chief, Experimental Therapeutics Branch  
National Institutes of Health  
Bethesda, Maryland  

†IRWIN C. WINTER, Ph.D., M.D.  
Vice President, Medical Affairs  
G. D. Searle & Co.  
Chicago, Illinois  

* Resigned, November 24, 1970  
† Ex-officio—as Chairman of Scientific Advisory Committee
<table>
<thead>
<tr>
<th>Name</th>
<th>Position and Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>WALTER F. RIKER, JR., M.D.</td>
<td>Chairman, Department of Pharmacology, Cornell University Medical College, New York</td>
</tr>
<tr>
<td>KURT BENIRSCHKE, M.D.</td>
<td>Professor and Chairman, Department of Obstetrics, University of California, San Diego</td>
</tr>
<tr>
<td>CLYDE G. CULBERTSON, M.D.</td>
<td>Pathologist and Research Advisor, The Lilly Research Laboratories, Eli Lilly and Company</td>
</tr>
<tr>
<td>KENNETH P. DUBOIS, Ph.D.</td>
<td>Director, Toxicity Laboratory, The University of Chicago, Chicago</td>
</tr>
<tr>
<td>DON W. FAWCETT, M.D.</td>
<td>Hersey Professor of Anatomy, Department of Anatomy, Harvard Medical School, Boston</td>
</tr>
<tr>
<td>CARLOS KOSMA, M.D.</td>
<td>Head, Department of Pathology and Toxicology, The Wellcome Research Laboratories, Burroughs Wellcome &amp; Co., Research Triangle Park, North Carolina</td>
</tr>
<tr>
<td>LEON Z. SAUNDERS, D.V.M., Ph.D.</td>
<td>Director, Pathology and Toxicology, Research and Development Division, Smith Kline &amp; French Laboratories, Philadelphia, Pennsylvania</td>
</tr>
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It is suggested that requests for assistance take the form of a letter, outlining the subject, purposes, scope, brief description of methods or procedures to be used, principal researchers, percentage of time to be devoted to project by each of the principals, curriculum vitae, bibliographies of the principal researchers, the budget, other sources of present or anticipated financing of this same undertaking, a listing by title of other research projects presently involved in by the principal researchers and the amount of time devoted to each, and the amount and source of funds for these activities. All of the above information must be supplied.

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